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(21) International Application Number: PCT/US99/13024

(22) International Filing Date: 11 June 1999 (11.06.1999)

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(26) Publication Language: English

(71) Applicant *(for all designated States except US)*: **THE TRUSTEES OF TUFTS COLLEGE** [US/US]; Packard Hall, Medford, MA 02155 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **GOLDBERG, Edward, B.** [US/US]; 494 Ward Street, Newton, MA 02459 (US).

(74) Agents: **ANTLER, Adriane, M.** et al.; Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY 10036 (US).

(81) Designated States *(national)*: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/77196 A1

(54) Title: GENE AND PROTEIN SEQUENCES OF PHAGE T4 GENE 35

(57) Abstract: The present invention relates to nucleotide sequences of gp35 genes and amino acid sequences of their encoded proteins, as well as derivatives and analogs thereof, and antibodies thereto. The present invention further relates to the use of nucleotide sequences of bacteriophage T4 gene 35 and amino acid sequences of its encoded protein, as well as derivatives, variants, and analogs thereof in the construction of nanostructures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/13024

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : C12N 15/11, 15/63, 15/85; C07K 14/00, 16/00
US CL : 536/23.1; 435/320.1, 325; 530/350, 387

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1; 435/320.1, 325; 530/350, 387

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DATABASE: APS; STN/CAS: Scisearch, Medline, Biosis, Caplus.
SEARCH TERM: Bacteriophage, T4 tail, GP35, p35, Antibody.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,864,013 A (GOLDBERG) 26 January 1999, see entire document.	1-48
A	US 5,877,279 A (GOLDBERG) 02 March 1999, see entire document.	1-48
X	WO 96/11947 A1 (GOLDBERG, E. B.) 25 April 1996, especially figure 7.	5
A	REVEL, H. R. Organization of the bacteriophage T4 tail fiber gene cluster 34-38. Proceedings of the Seventh Biennial Conference on Bacteriophage Assembly. September 1980, pages 353-364, see entire document.	1-48

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
15 SEPTEMBER 1999

Date of mailing of the international search report
29 OCT 1999

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
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Authorized officer
SUMESH KAUSHAL
Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/13024

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DICKSON, R. C. Assembly of bacteriophage T4 tail fibers. Journal of Molecular Biology. October 1973, Vol. 79, No. 4, pages 633-647, see entire document.	1-48
A	REVEL, H. R. Molecular cloning of the T4 genome: organisation and expression of the tail fiber gene cluster 34-38. Molecular and General Genetics. 1981, Vol. 182, No. 3, pages 445-445, see entire document.	1-48
X	OLIVER, D. B. DNA sequence of the tail fibre genes *36* and *37* of bacteriophage T4. Journal of Molecular Biology. 1981, Vol. 153, pages 545-568, especially Sequence VG35_BPT4.	6

ATENT COOPERATION TRE TY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 03 April 2001 (03.04.01)	
International application No. PCT/US99/13024	**Applicant's or agent's file reference** 8471-007-228
International filing date (day/month/year) 11 June 1999 (11.06.99)	**Priority date** (day/month/year)
Applicant GOLDBERG, Edward, B.	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

04 January 2001 (04.01.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

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1636

10/009874

PATENT COOPERATION TREATY

RECD 08 JAN 2002
WIPO PCT

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

12

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of Internation Preliminary Examination Report (Form PCT/IPEA/41
8471-007-228		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/13024	11 JUNE 1999	NONE

International Patent Classification (IPC) or national classification and IPC
Please See Supplemental Sheet.

Applicant
THE TRUSTEES OF TUFTS COLLEGE

1. This international preliminary examination report has been prepared by this International Preliminar Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which h been amended and are the basis for this report and/or sheets containing rectifications made before this Author (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 5 sheets.

RECEIVED
MAY 17 2002
TECH CENTER 1600/2900

3. This report contains indications relating to the following items:

- I [X] Basis of the report
- II [ ] Priority
- III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV [ ] Lack of unity of invention
- V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicabilit citations and explanations supporting such statement
- VI [ ] Certain documents cited
- VII [ ] Certain defects in the international application
- VIII [ ] Certain observations on the international application

TECH CENTER 1600/2900

Date of submission of the demand	Date of completion of this report
04 JANUARY 2001	29 NOVEMBER 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer SUMESH KAUSHAL
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/13024

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the claims:
pages (See Attached) , as originally filed
pages _____ , as amended (together with any statement) under Article 19
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the drawings:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the sequence listing part of the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in whic the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which i

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 ai or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the internationa preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. 47-48

☒ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/13024

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-46	YE
	Claims	none	NO
Inventive Step (IS)	Claims	1-46	YE
	Claims	none	NO
Industrial Applicability (IA)	Claims	1-46	YE
	Claims	none	NO

2. citations and explanations (Rule 70.7)

Claims 1-46, meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a composition comprising at least 1 microgram of a purified nodenatured gp35 protein, wherein the composition is not a gel. The prior art does not teach or suggest the claimed variant of gp35 and method of making the variants in recombinant host cells. In addition the prior art does not teach or suggest the a kit comprising nucleic acid primers capable of amplification of a gp35 gene in which 5' primer is upstream of or comprising a sequence encoding the N-terminus of the gp35 protein.

---------- NEW CITATIONS ----------
NONE

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 15/11, 15/63, 15/85; C07K 14/00, 16/00 and US Cl.: 536/23.1; 435/320.1, 325; 530/350, 387

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-44, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) NONE, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand.
and additional amendments:
Pages 45-49, filed with the letter of 30 July 2001

This report has been drawn on the basis of the drawings,
page(s) 1-22, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) NONE, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

WHAT IS CLAIMED IS:

1. A composition comprising at least 1 microgram of a purified nondenatured gp35 protein, with the proviso that said composition is not a gel.

2. A purified bacteriophage T4 gp35 protein that is not contained in a gel.

3. A purified protein comprising the amino acid sequence depicted in Figure 2 (SEQ ID NO:2) with one or more conservative substitutions relative to said sequence, wherein the purified protein is not contained in a gel.

4. A purified protein comprising an amino acid sequence of 100 amino acids that has at least 60% identity to a gp35 protein having the amino acid sequence depicted in Figure 2 (SEQ ID NO:2), wherein the purified protein is not contained in a gel.

5. A purified protein comprising at least 8 contiguous amino acids of the gp35 protein sequence depicted in Figure 2 (SEQ ID NO:2) from amino acids numbers 1 to 24, and which displays one or more functional activities of a gp35 protein, wherein the purified protein is not contained in a gel.

6. The protein of claim 5 which is able to be bound by an antibody directed against a gp35 protein.

7. The protein of claim 5 which has only conservative substitutions relative to the sequence in Figure 2 (SEQ ID NO:2).

8. A molecule comprising the protein of claim 5.

9. The protein of claim 4 which specifically binds with the P34 protein oligomer of bacteriophage T4.

10. A purified fragment of the protein of claim 4, which comprises at least 8 contiguous amino acids of the gp35 protein sequence depicted in Figure 2 (SEQ ID NO:2)

from amino acids numbers 1 to 24, and which displays one or more functional activities of a gp35 protein.

11. The fragment of claim 10 which is able to be bound by an antibody directed against a gp35 protein.

12. A purified protein variant of a gp35 protein of bacteriophage T4, that is able to be bound by an antibody directed against a gp35 protein, wherein the interaction of said variant with the P36 protein oligomer of bacteriophage T4 is unstable at temperatures between about 40°C and about 60°C.

13. A purified protein variant of a gp35 protein of bacteriophage T4, that is able to be bound by an antibody directed against a gp35 protein, wherein the interaction of said variant with the P34 protein oligomer of bacteriophage T4 is unstable at temperatures between about 40°C and about 60°C.

14. A purified protein variant of a gp35 protein of bacteriophage T4, that (a) is able to be bound by an antibody directed against a gp35 protein, and (b) is conjugated to a group that confers the ability of the variant to bind a ligand.

15. The variant of claim 14, wherein said ligand is selected from the group consisting of avidin, immunoglobulin, and a divalent metal ion.

16. A purified molecule comprising a bacteriophage T4 gp35 protein fragment, wherein said fragment consists of at least the amino acid sequence depicted in Figure 2 (SEQ ID NO:2) from amino acids numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 or 81-93.

17. A purified molecule comprising the amino acid sequence depicted in Figure 2 (SEQ ID NO:2) from amino acids numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 or 81-93, with one or more conservative substitutions relative to said sequence.

18. A purified molecule comprising an amino acid sequence having at least 30% identity to amino acids numbers 57 to 93 in Figure 2 (SEQ ID NO:2) over a 36 amino acid sequence, wherein the purified molecule is not contained in a gel.

19. A purified protein having at least 60% identity to amino acids numbers 57 to 93 in Figure 2 (SEQ ID NO:2) over a 36 amino acid sequence, wherein the purified protein is not contained in a gel.

20. A purified protein comprising at least a functionally active portion of the amino acid sequence in Figure 2 (SEQ ID NO:2) from amino acids numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-64, 66-79, or 81-93, wherein the purified protein is not contained in a gel.

21. A purified molecule comprising an amino acid sequence having at least 60% identity to amino acids numbers 1 to 100 in Figure 2 (SEQ ID NO:2) over a 100 amino acid sequence, wherein the purified protein is not contained in a gel.

22. The purified fragment of claim 5, wherein said fragment lacks at least 10 contiguous amino acids of the sequence depicted in Figure 2 (SEQ ID NO:2).

23. A purified nucleic acid, comprising a nucleotide sequence encoding a gp35 protein having the amino acid sequence depicted in Figure 2 (SEQ ID NO: 2), operably linked to a heterologous promoter that controls expression of the nucleotide sequence.

24. A purified nucleic acid, comprising a nucleotide sequence encoding a gp35 protein having the amino acid sequence depicted in Figure 2 (SEQ ID NO: 2), contiguous with a sequence of at least 10 nucleotides that is not of bacteriophage T4.

25. The purified nucleic acid of claim 23, further comprising nucleotide sequences encoding gp36, gp37 and gp57 proteins, respectively, operably linked to said promoter.

26. The purified nucleic acid of claim 23, in which the nucleic acid is DNA.

27. The purified nucleic acid of claim 23, in which the nucleic acid is RNA.

28. A purified nucleic acid comprising a nucleotide sequence absolutely complementary to a nucleotide sequence encoding a gp35 protein having the amino acid sequence depicted in Figure 2 (SEQ ID NO:2), contiguous with a sequence of at least 10 nucleotides that is not of bacteriophage T4.

29. A purified nucleic acid comprising at least 850 contiguous nucleotides of a *gp35* DNA sequence, with the proviso that the nucleic acid does not contain a bacteriophage T4 promoter.

30. A purified nucleic acid, comprising a nucleotide sequence encoding a gp35 protein consisting of at least the amino acid sequence shown in Figure 2 from amino acids numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79, or 81-93.

31. A purified nucleic acid comprising a nucleotide sequence encoding a protein consisting of at least the amino acid sequence shown in Figure 2 (SEQ ID NO:2) from amino acids numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-93, 57-64, 66-79 or 81-93, with one or more conservative substitutions relative to said sequence.

32. A purified nucleic acid, comprising the nucleotide sequence depicted in Figure 2 (SEQ ID NO:1) from nucleotide numbers 1 to 1,116, wherein said sequence is contiguous to a 3′ termination codon.

33. A purified nucleic acid, comprising a nucleotide sequence encoding a protein having at least 30% identity to amino acids numbers 57 to 93 in Figure 2 (SEQ ID NO:2) over a 36 amino acid sequence.

34. A purified nucleic acid, comprising a nucleotide sequence encoding a protein containing at least a functionally active portion of the amino acid sequence in Figure 2 from amino acids numbers 1-17, 1-56, 1-78, 1-93, 8-17, 57-64, 66-79, or 81-93.

35. A purified nucleic acid, comprising a nucleotide sequence encoding the protein of claim 10.

36. The purified nucleic acid of claim 35, wherein said protein is missing at least 10 contiguous amino acids of the sequence depicted in Figure 2 (SEQ ID NO:2).

37. A nucleic acid vector comprising the nucleic acid of claim 24 or 31.

38. An expression vector comprising the nucleic acid of claim 31 operably linked to a heterologous promoter that controls expression of the nucleotide sequence in a host cell.

39. A host cell that contains the nucleic acid of claim 23.

40. A host cell that contains the nucleic acid of claim 31.

41. A host cell that contains the nucleic acid of claim 31 operably linked to a heterologous promoter that controls expression of the nucleotide sequence in the host cell.

42. A method of producing a protein comprising growing the host cell of claim 39 such that the gp35 protein is expressed by the cell, and recovering the expressed protein.

43. A method of producing a protein comprising growing the host cell of claim 41 such that the encoded protein is expressed by the cell, and recovering the expressed protein.

44. The product of the method of claim 42.

45. The product of the method of claim 43.

46. A kit comprising in one or more containers a pair of nucleic acid primers capable of priming amplification of at least a portion of a gp35 gene, in which the 5′ primer is upstream of or comprising a sequence encoding the N-terminus of a gp35 protein.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

1725

To: ADRIANE M. ANTLER
PENNIE & EDMONDS LLP
1155 AVENUE OF THE AMERICAS
NEW YORK, NEW YORK 10036

REFERRED TO Antler
REC'D Schneiderman
JUL 02 2001
Pennie & Edmonds
O.K. for filing

PCT

WRITTEN OPINION

(PCT Rule 66)

Written Opinion: 7/28/01 (GM)

Date of Mailing *(day/month/year)*	28 JUN 2001
Applicant's or agent's file reference: 8471-007-228	REPLY DUE within ONE months from the above date of mailing
International application No.: PCT/US99/13024	International filing date *(day/month/year)*: 11 JUNE 1999
Priority date *(day/month/year)*: NONE	
International Patent Classification (IPC) or both national classification and IPC: Please See Supplemental Sheet.	
Applicant: THE TRUSTEES OF TUFTS COLLEGE	

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
   - I [X] Basis of the opinion
   - II [ ] Priority
   - III [ ] Non-establishment of opinion with regard to novelty, inventive step or industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [X] Certain observations on the international application
3. The applicant is hereby invited to reply to this opinion.
   When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension., see Rule 66.2(d).~~
   How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.
   Also For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*. For an informal communication with the examiner, see Rule 66.6.
   If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.
4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 11 OCTOBER 2001

Name and mailing address of the IPEA/US: Commissioner of Patents and Trademarks, Box PCT, Washington, D.C. 20231	Authorized officer: SUMESH KAUSHAL / TERRY J. DEY PARALEGAL SPECIALIST TECHNOLOGY CENTER 1600
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/IPEA/408 (cover sheet) (July 1998) *

WRITTEN OPINION

International application No.
PCT/US99/13024

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-44 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 45-50 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages 1-22 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

[X] contained in the international application in printed form.

[X] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*

WRITTEN OPINION

International application No.
PCT/US99/13024

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-4, 7-48	YES
	Claims	5-6	NO
Inventive Step (IS)	Claims	1-4, 7-48	YES
	Claims	5-6	NO
Industrial Applicability (IA)	Claims	1-48	YES
	Claims	none	NO

2. citations and explanations

Claims 5 lack novelty under PCT Article 33(2) as being anticipated by Goldberg (WO96/11947, 1996). Goldburg teaches a nucleic acid molecule (fig-7), which hybridize to SEQ ID NO:1 of instant application with 96.3% sequence homology including open reading frames coding four polypeptides gp34, gp35, gp36 and gp37(see PTO sequence search report). Thus, the cited prior art clearly anticipate the invention as claimed.

Claims 6 lack novelty under PCT Article 33(2) as being anticipated by Oliver (J. Mol. Biol, 153:545-568, 1981). Oliver teaches an amino acid sequnce comprising 100 amino acids of tail fibre genes of bactariophage T4 that has 74.5% identity to the amino acid sequences of SEQ ID NO:2 of instant application (see PTO sequences search report). Thus the invention as claimed is clearly anticipated by the cited prior art.

Claims 1-4, and 7-48 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a composition comprising at least 1 microgram of a purified nodenatured gp35 protein, wherein the composition is not a gel. The prior art does not teach or suggest the claimed variant of gp35 and method of making the variants in recombinant host cells. In addition the prior art does not teach or suggest the a kit comprising nucleic acid primers capable of amplification of a gp35 gene in which 5' primer is upstream of or comprising a sequence encoding the N-terminus of the gp35 protein.

---------- NEW CITATIONS ----------
NONE

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to contain an adequate written description of the claimed purified proteins encoded by any and all variants of amino acid sequences of SEQ ID NO:2 and/or nucleic acid of SEQ ID NO:1. The description is inadequate because the description describes only the sequences SEQ ID No. 1 and SEQ ID No. 2 which encodes a bacteriophage T4 gp35 protein, wherein the invention as claimed encompasses any and all gp35-like proteins encoded by any and all variant of SEQ ID NO:1 and 2. The two sequences described do not reflect the genus of the purified proteins as claimed.

WRITTEN OPINION

International application No.
PCT/US99/13024

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 15/11, 15/63, 15/85; C07K 14/00, 16/00 and US Cl.: 536/23.1; 435/320.1, 325; 530/350, 387